

Figure 1

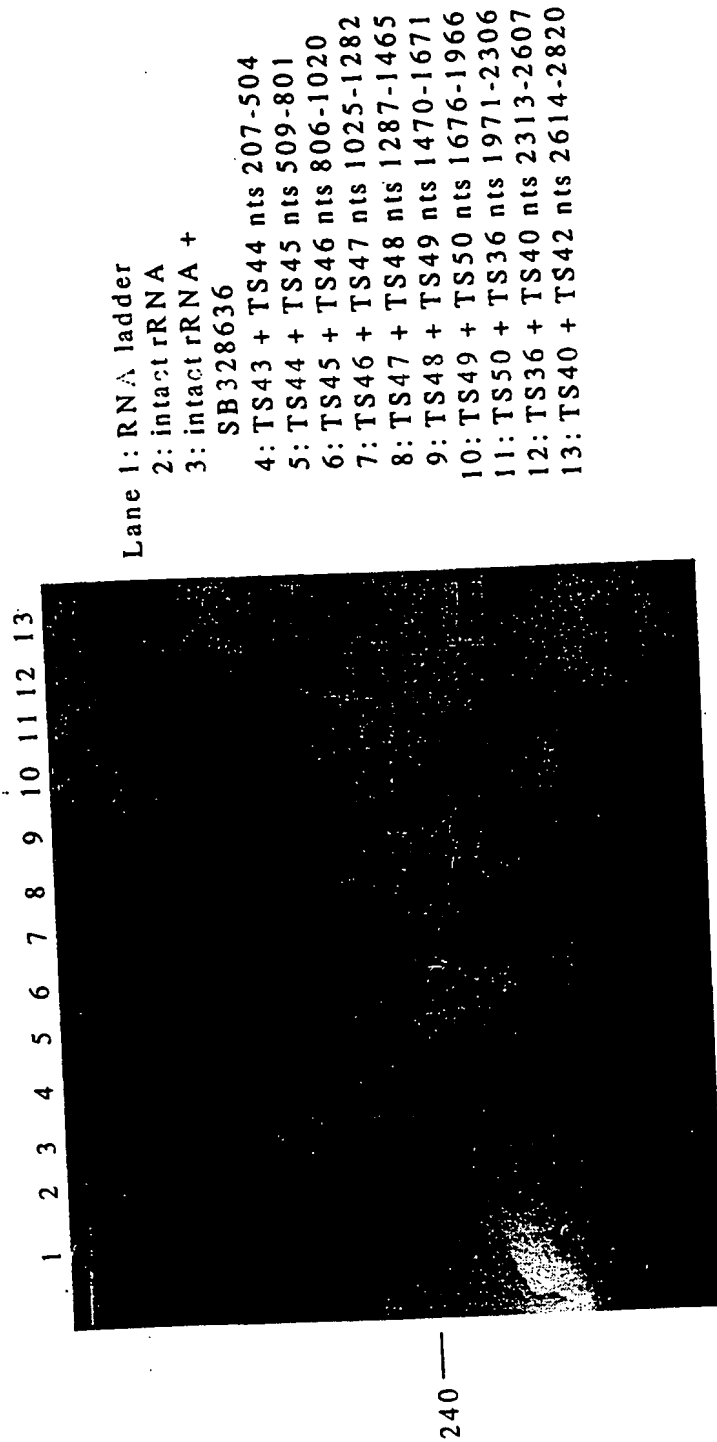


Figure 2

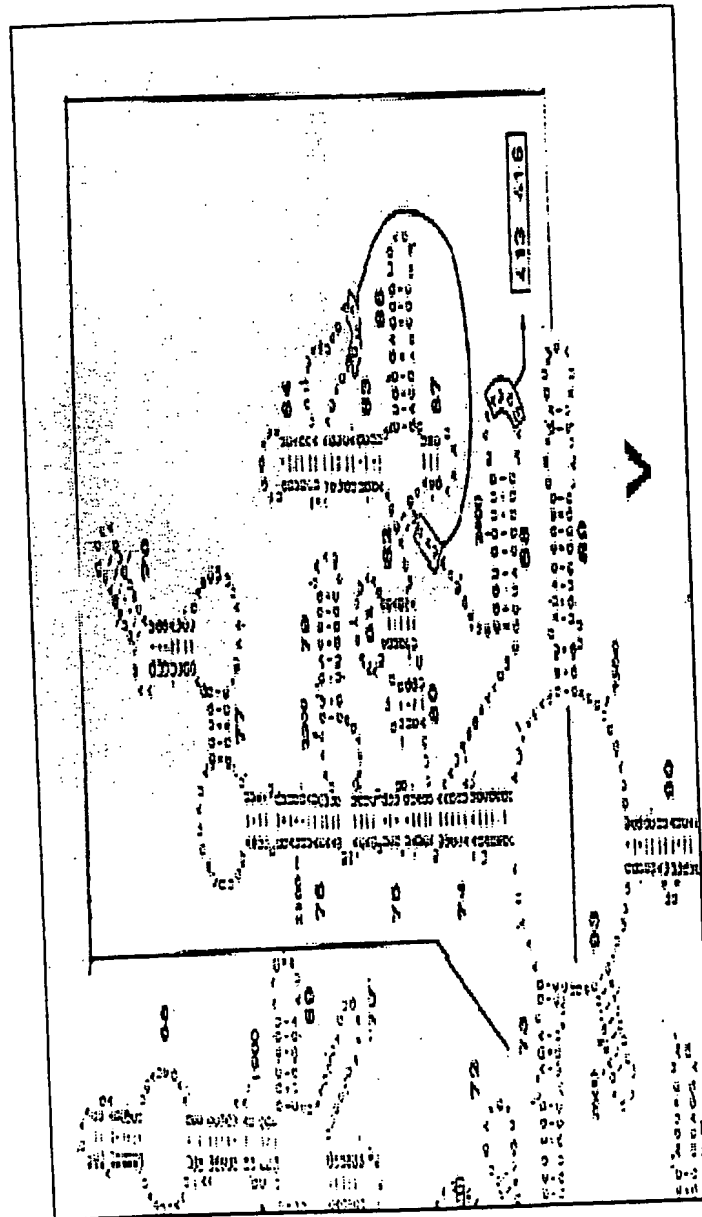
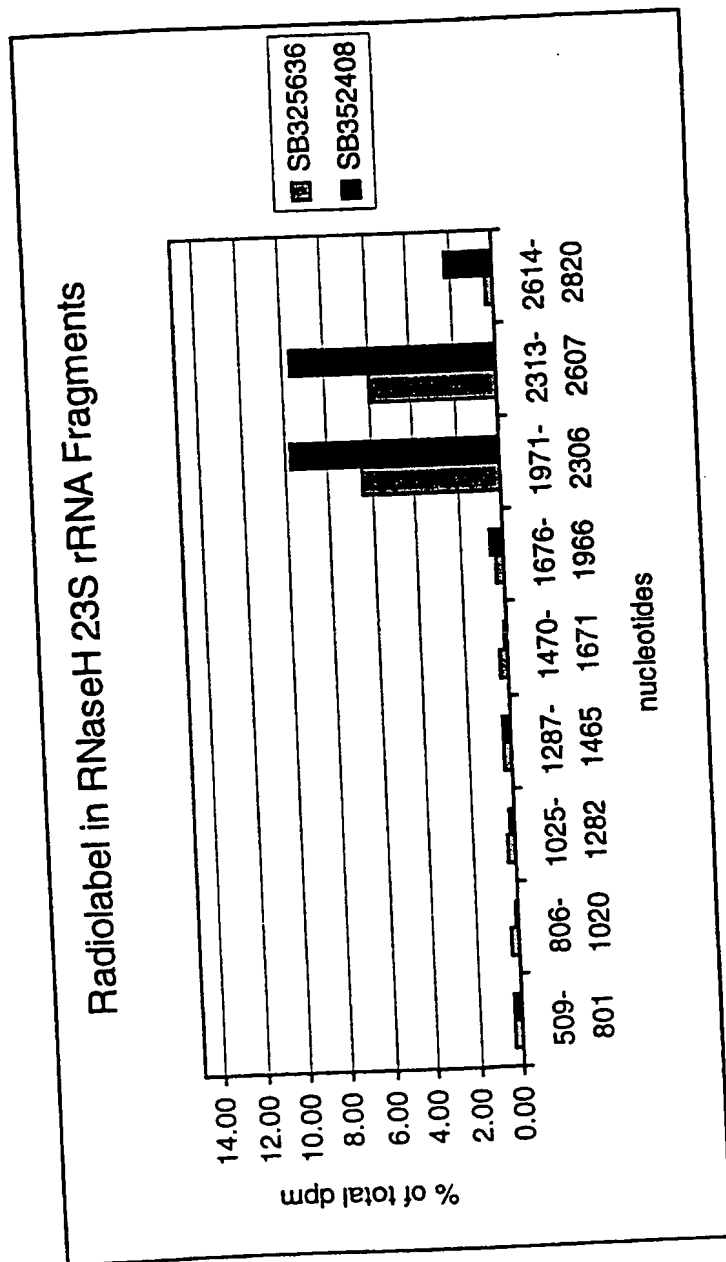
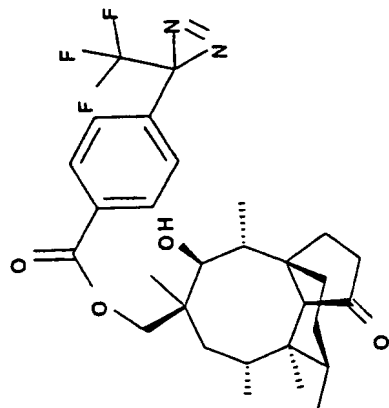


Figure 3



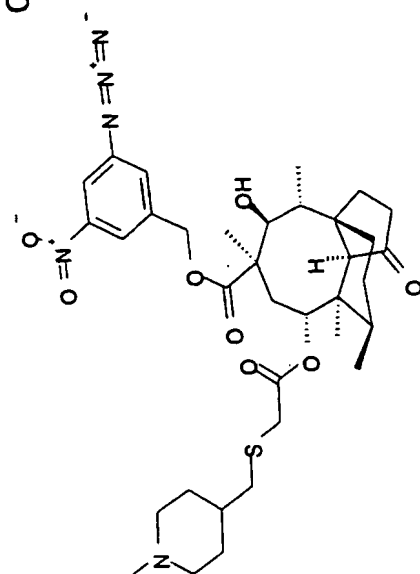
**Figure 4**

Chiral



SB-352408

Chiral



SB-328636

Figure 5

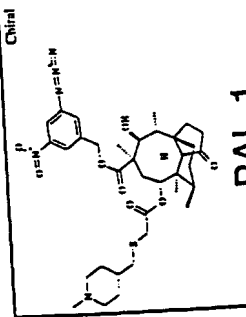
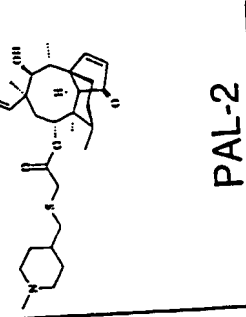
	 <p>Chiral</p>	 <p>Chiral</p>	PAL-2
RLB IC50 (uM)			0.54
S30 fmet IC50 (uM)			TBD
MICs (ug/mL)			
Organism			
<i>E. coli</i> DC0	>64		>64
<i>E. coli</i> DC2	64		8
<i>H. influenzae</i> Q1	>64		0.5
<i>M. catarrhalis</i> 1502	0.25		≤ 0.06
<i>E. faecalis</i> 1	>64		>64
<i>S. aureus</i> Oxford	2		0.25
<i>S. pneumoniae</i> R6	16		≤ 0.06
<i>S. pyogenes</i> CN 10	2		≤ 0.06

Figure 6.

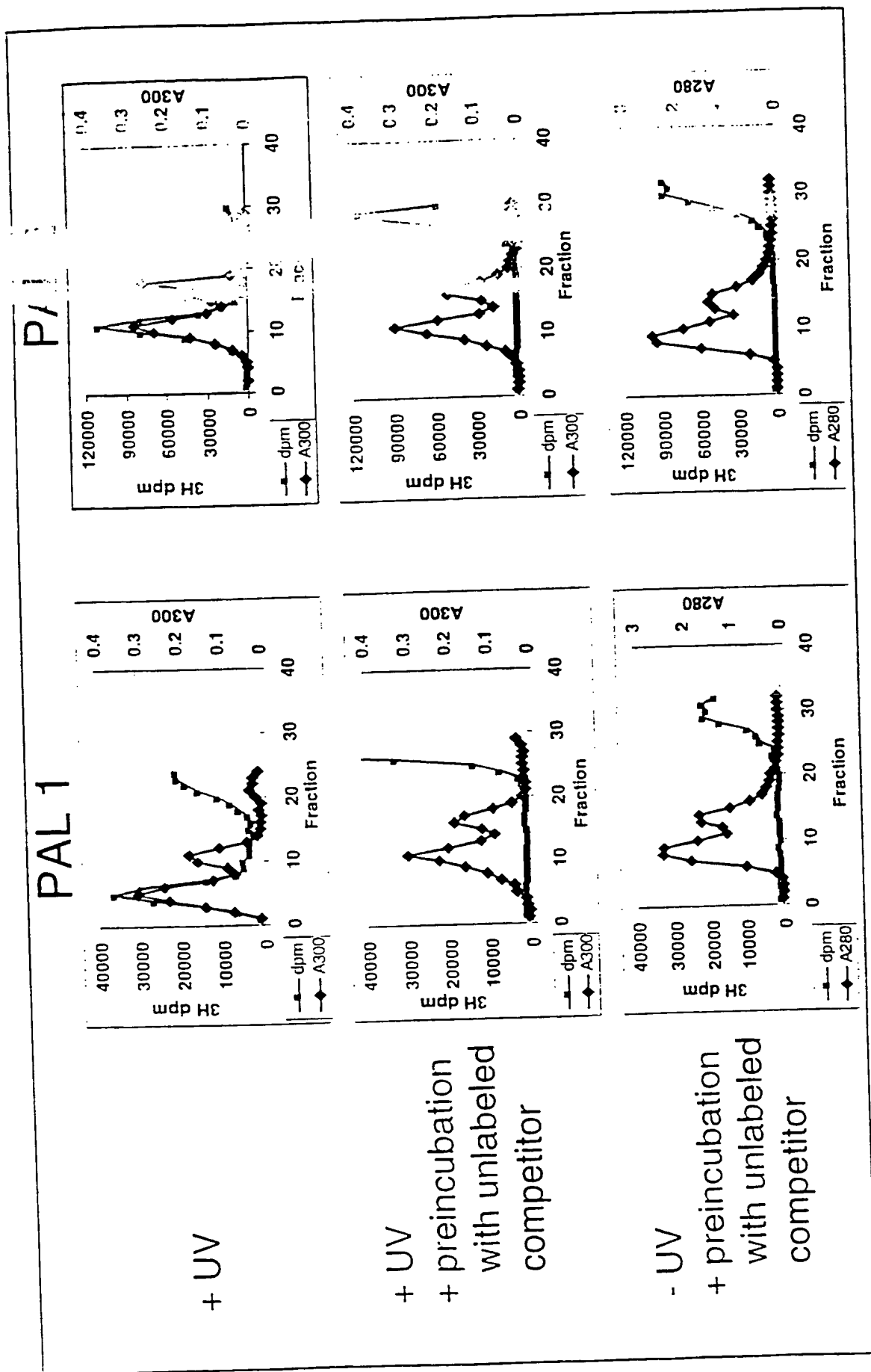
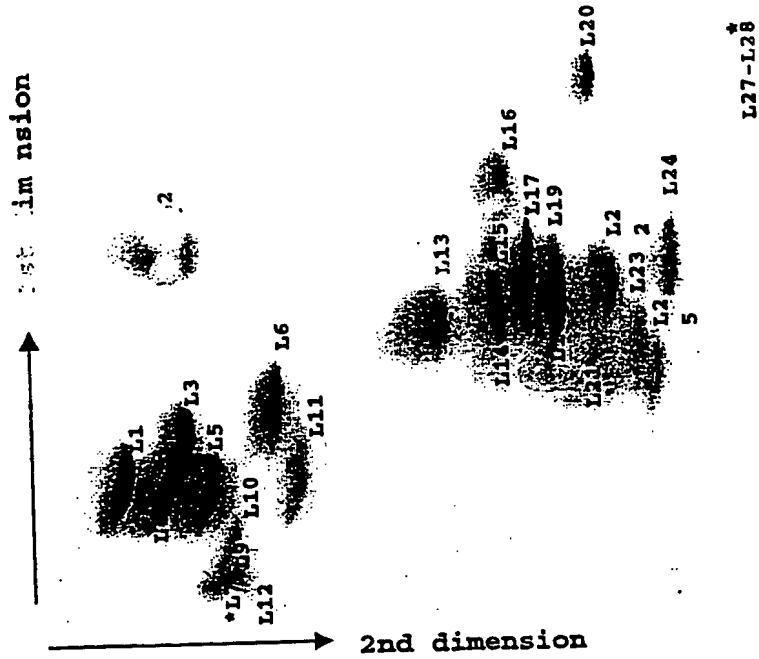


Figure 7.



\* L7, L12, L27, and L28 are seen with larger protein loads.

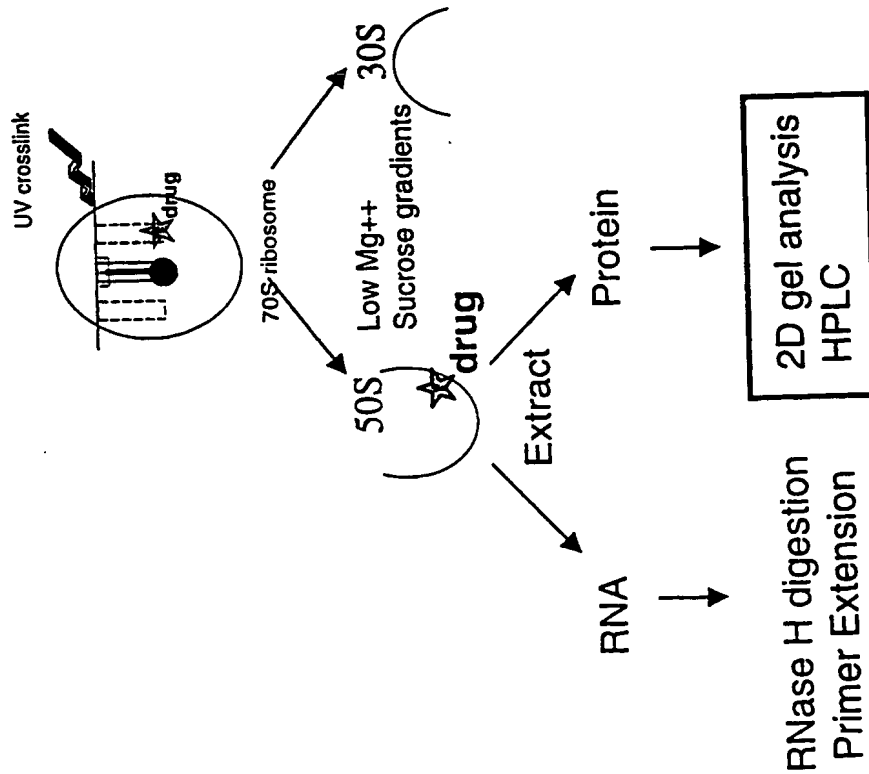


Figure 8.

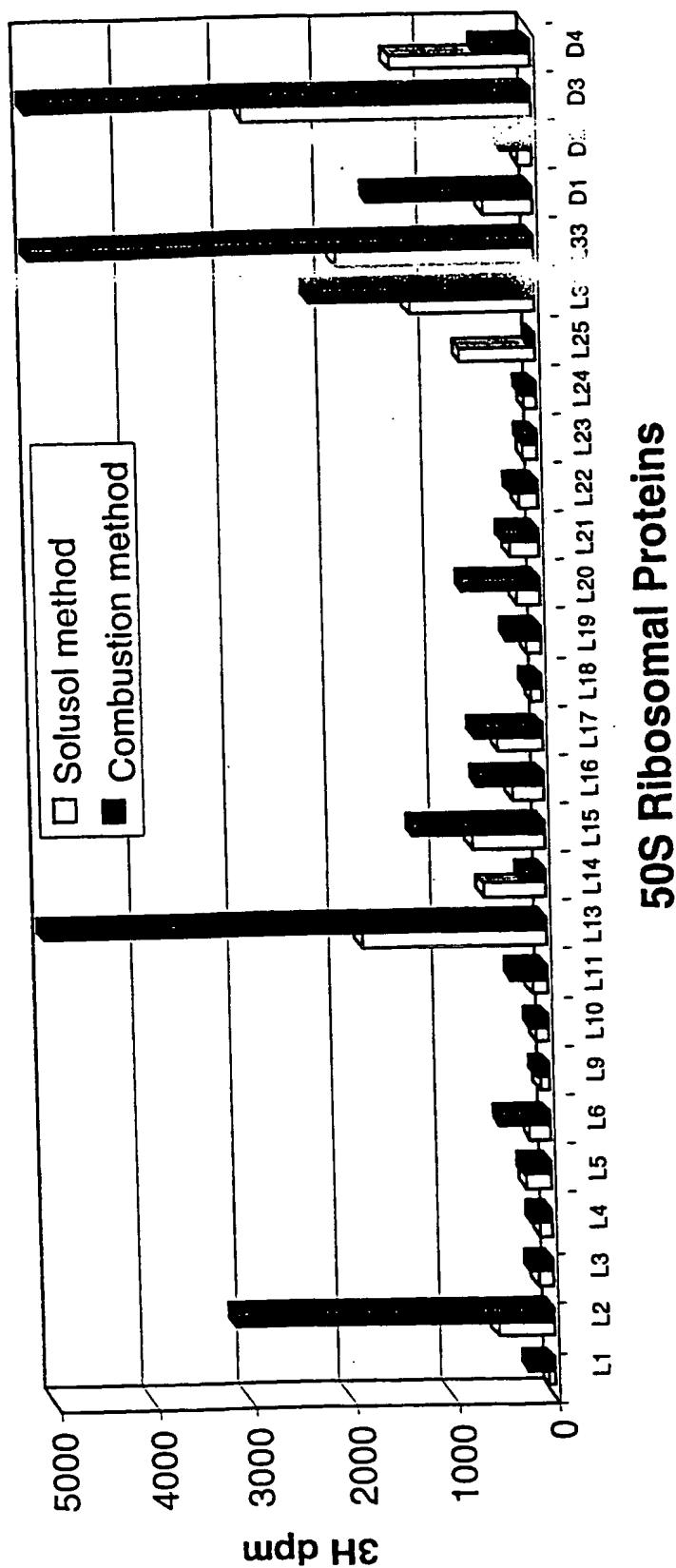


Figure 9.

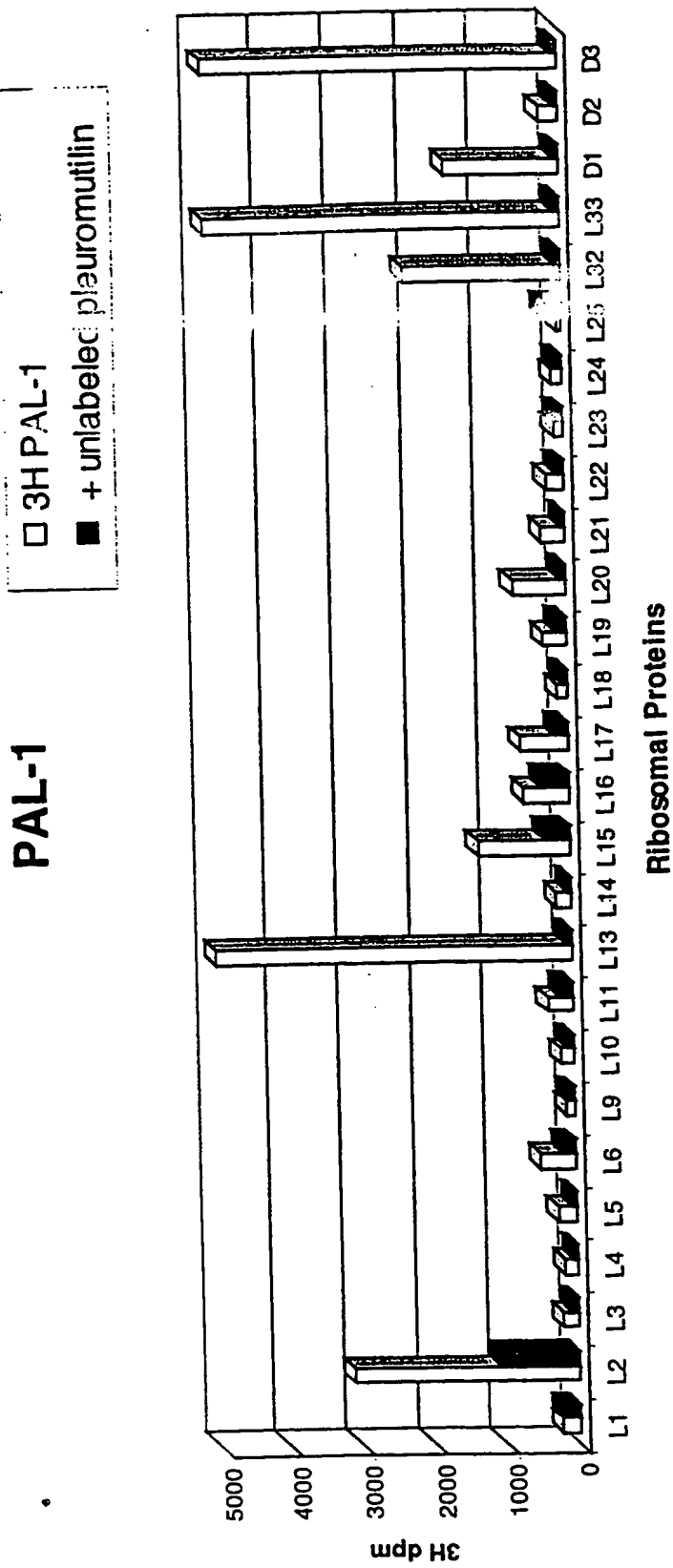


Figure 10.

# PAL-2

□ 3H PAL-2  
■ + unlabeled pleuromutilin

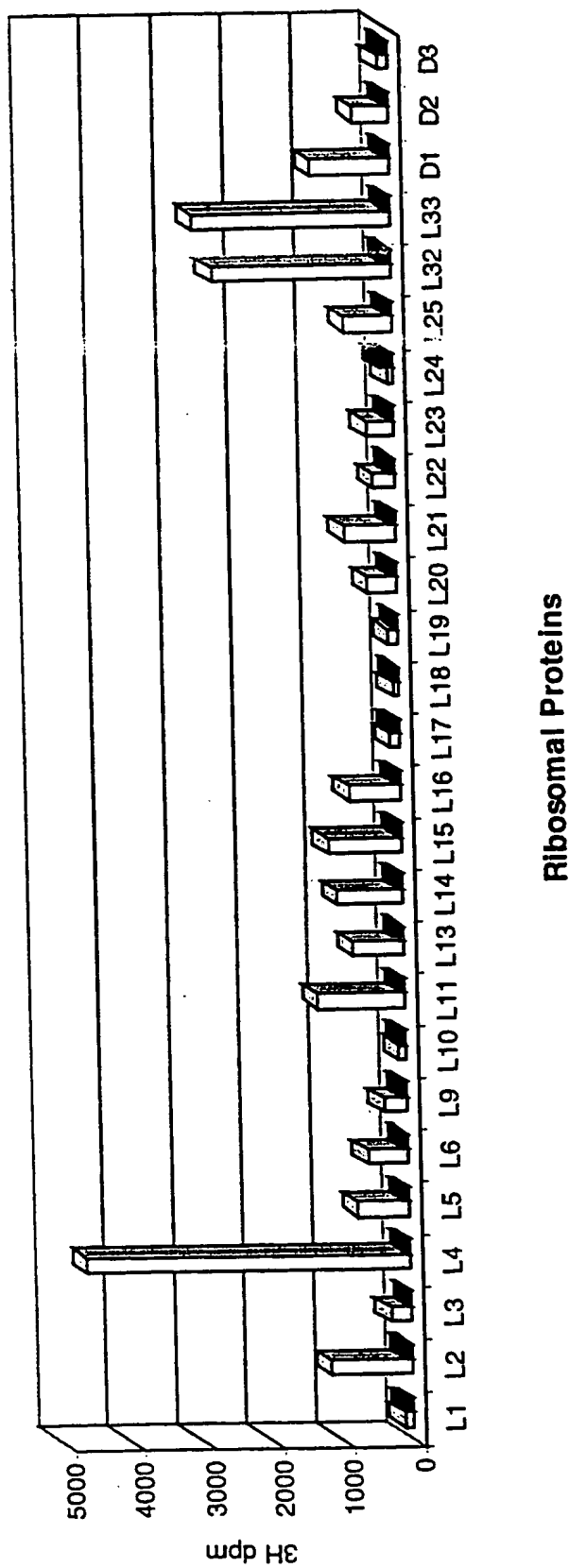
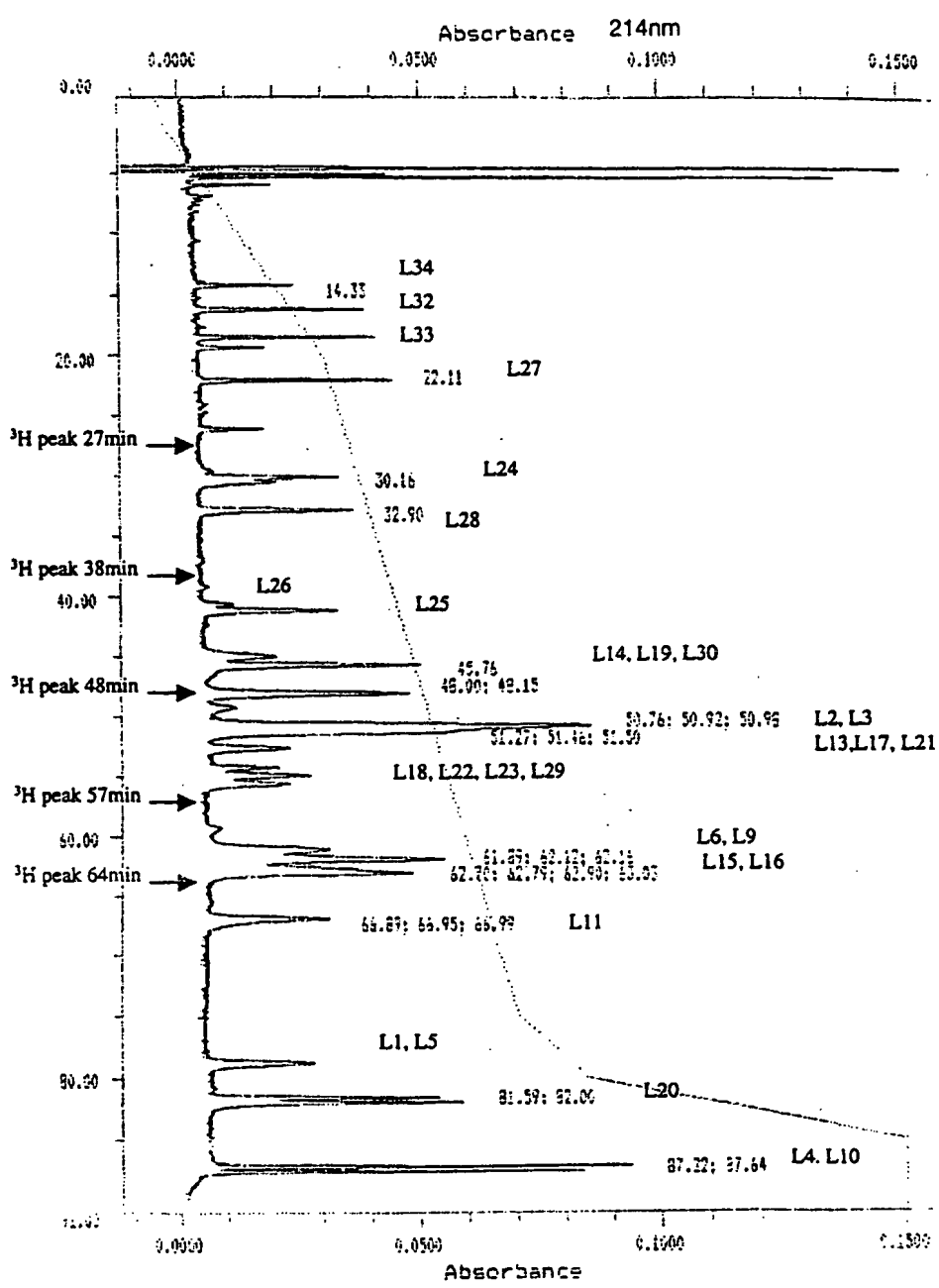


Figure 11.

Figure 12.



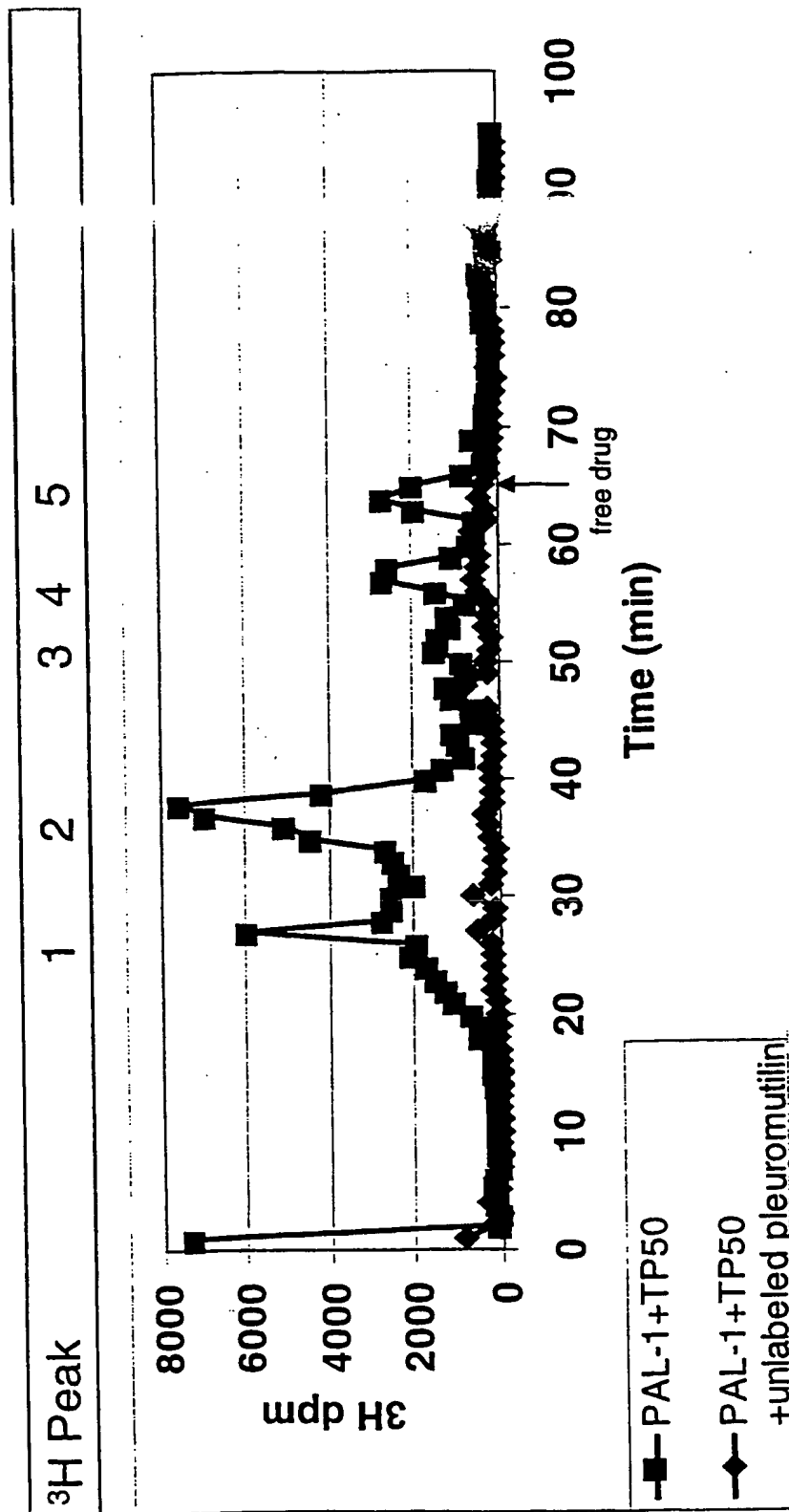
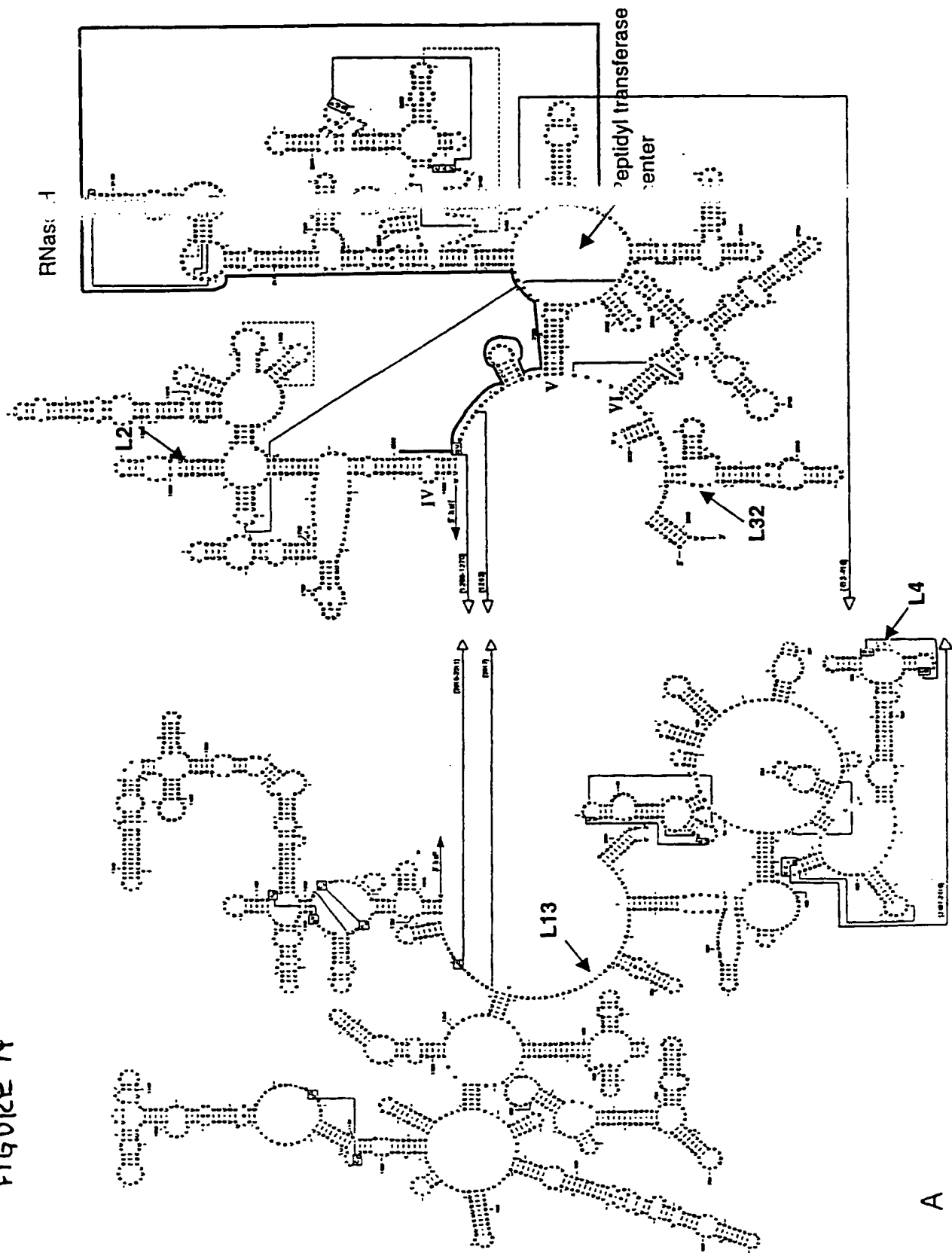
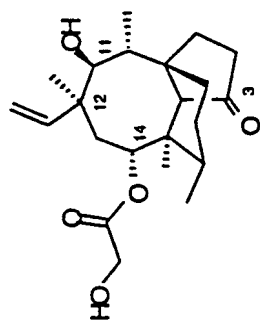


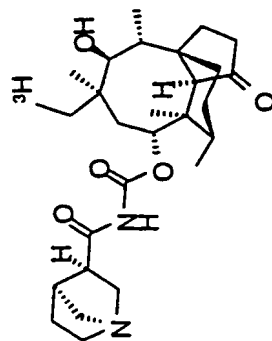
Figure 13.

FIGURE 14

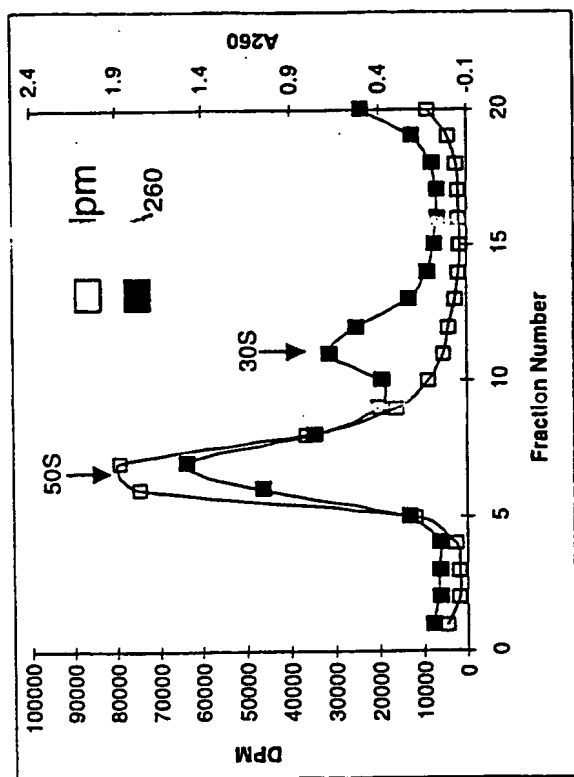




(A)



(B)



(C)

Fig 15.

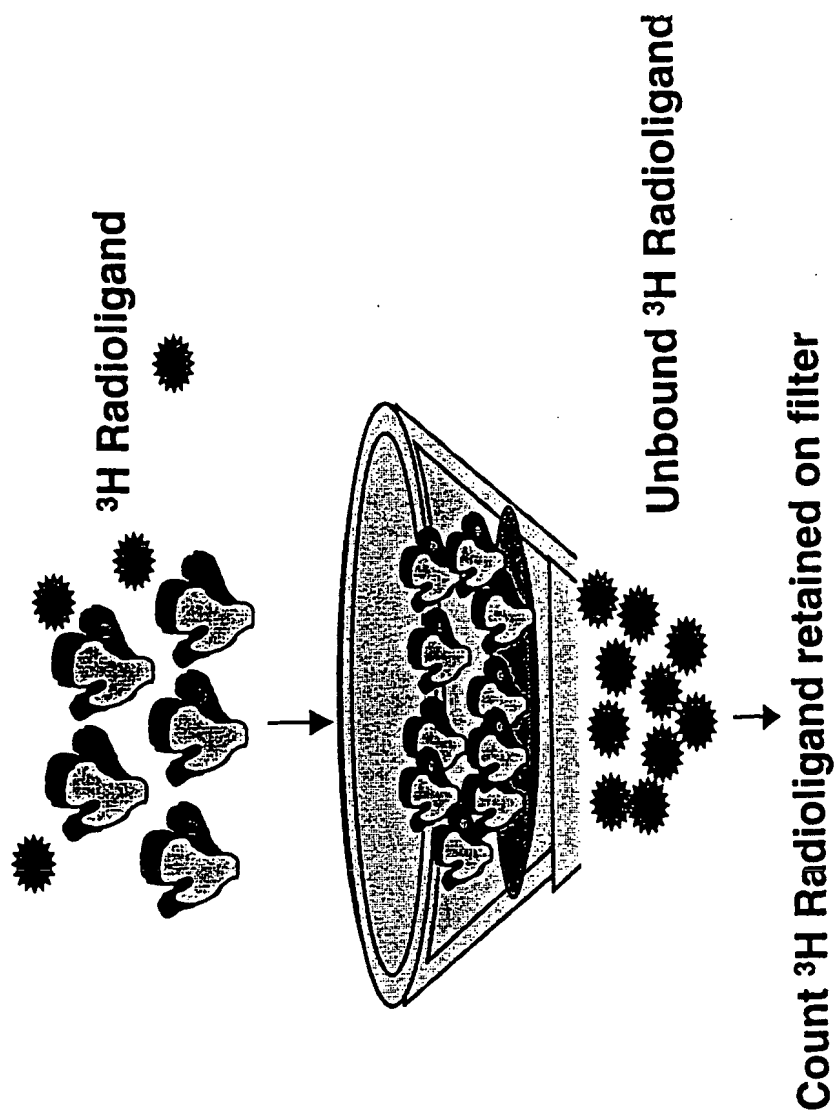


Figure 16..

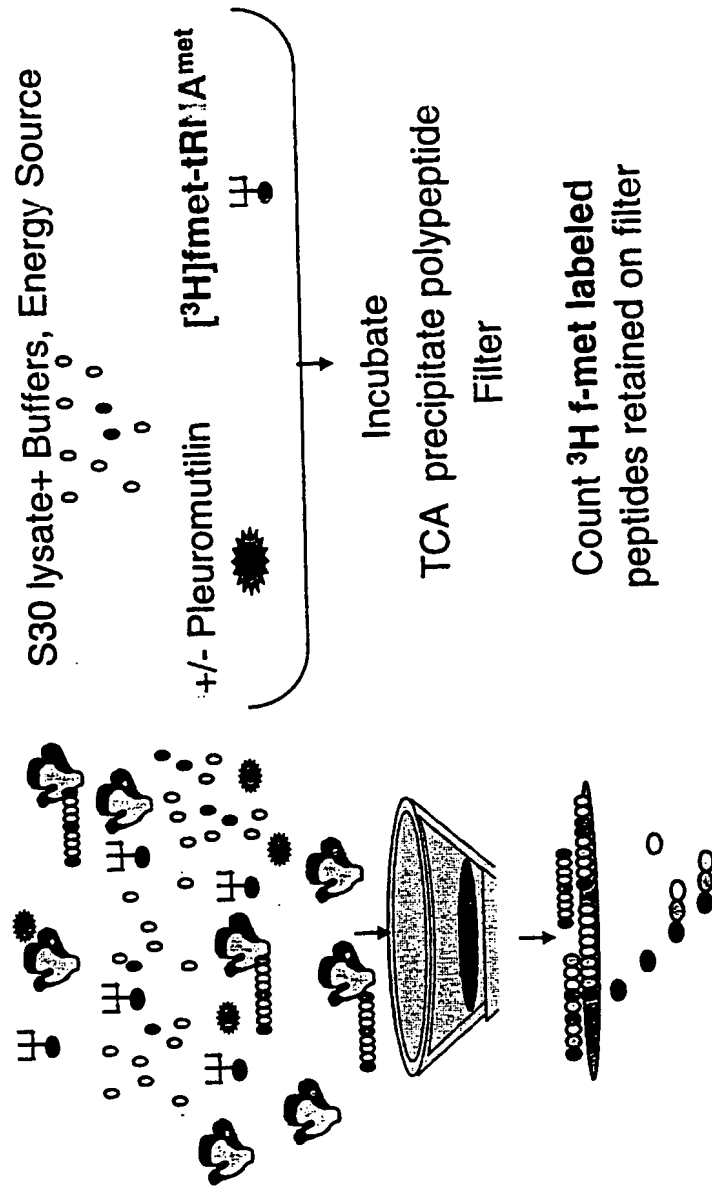


Figure 17.

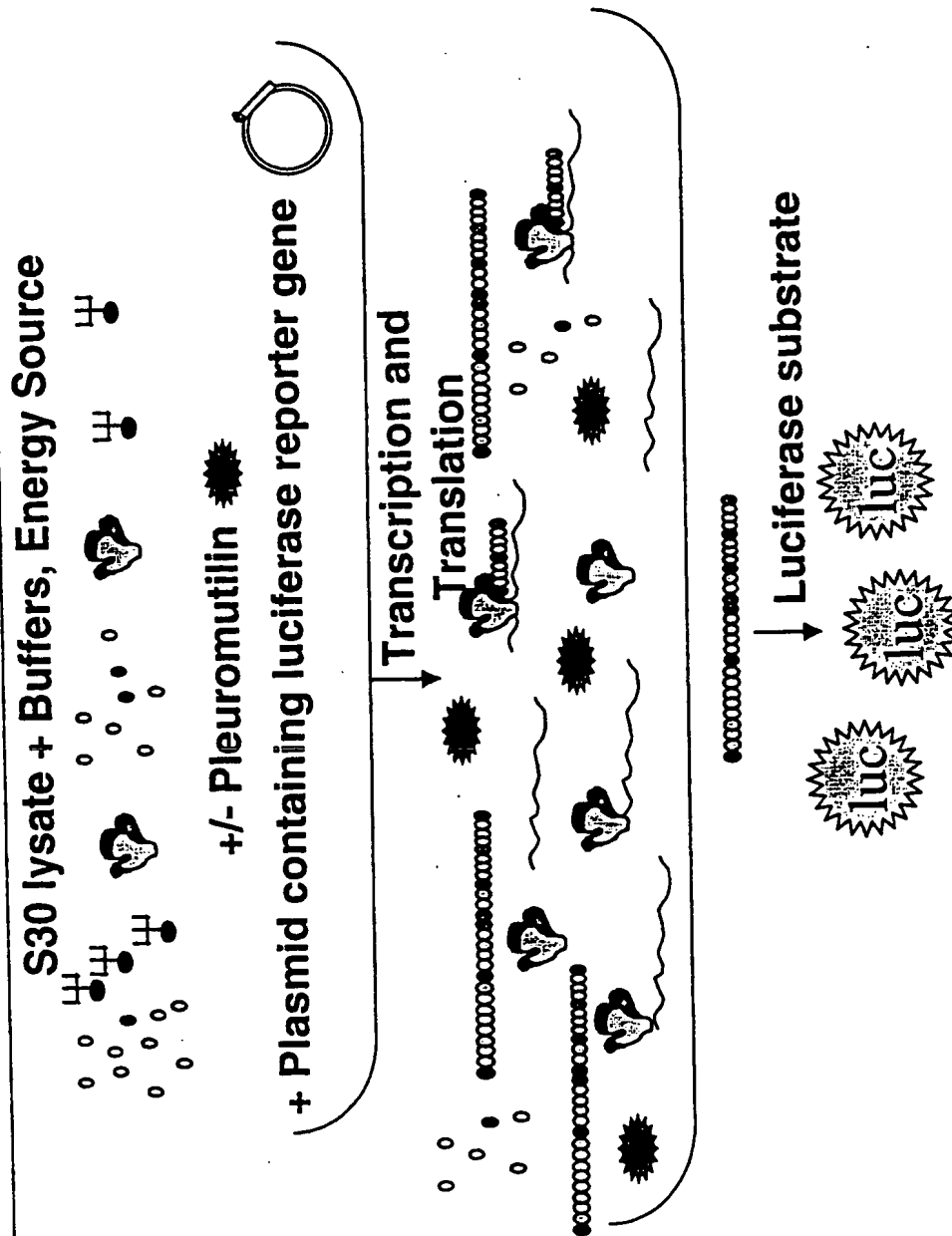


Figure 18.

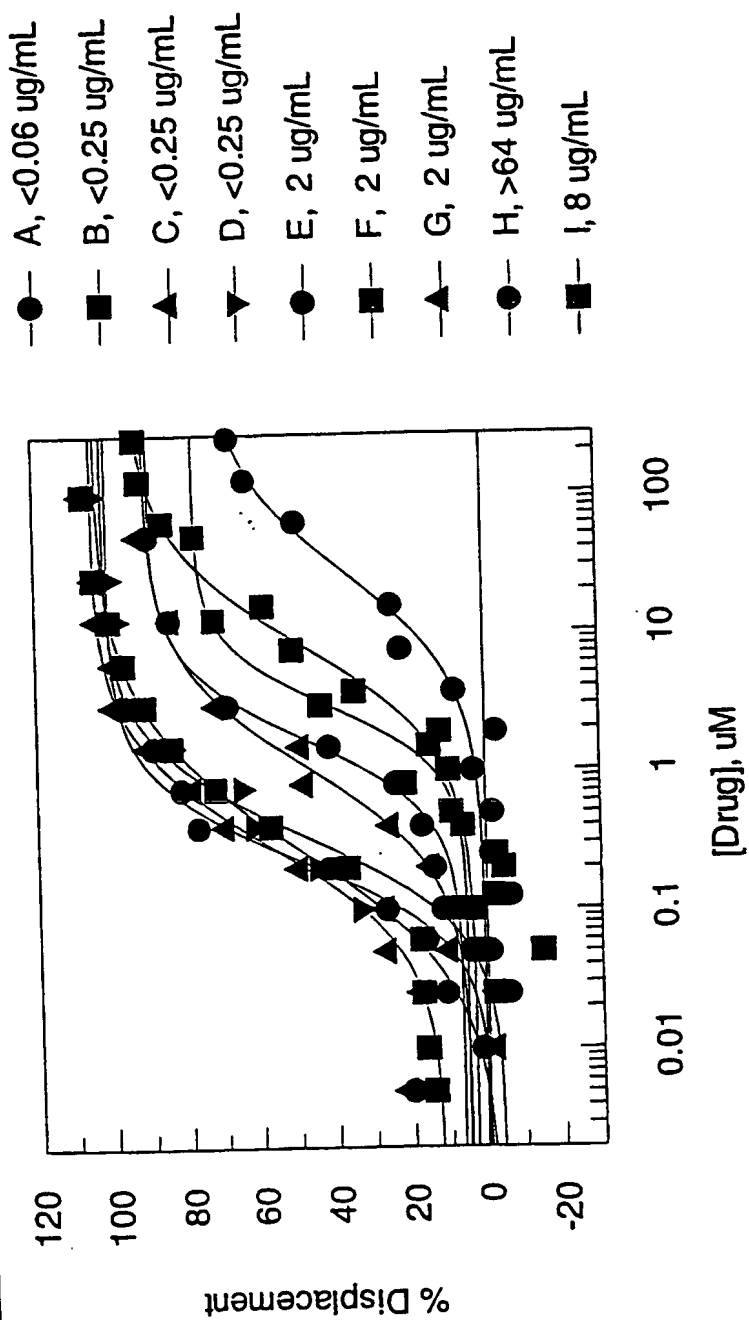
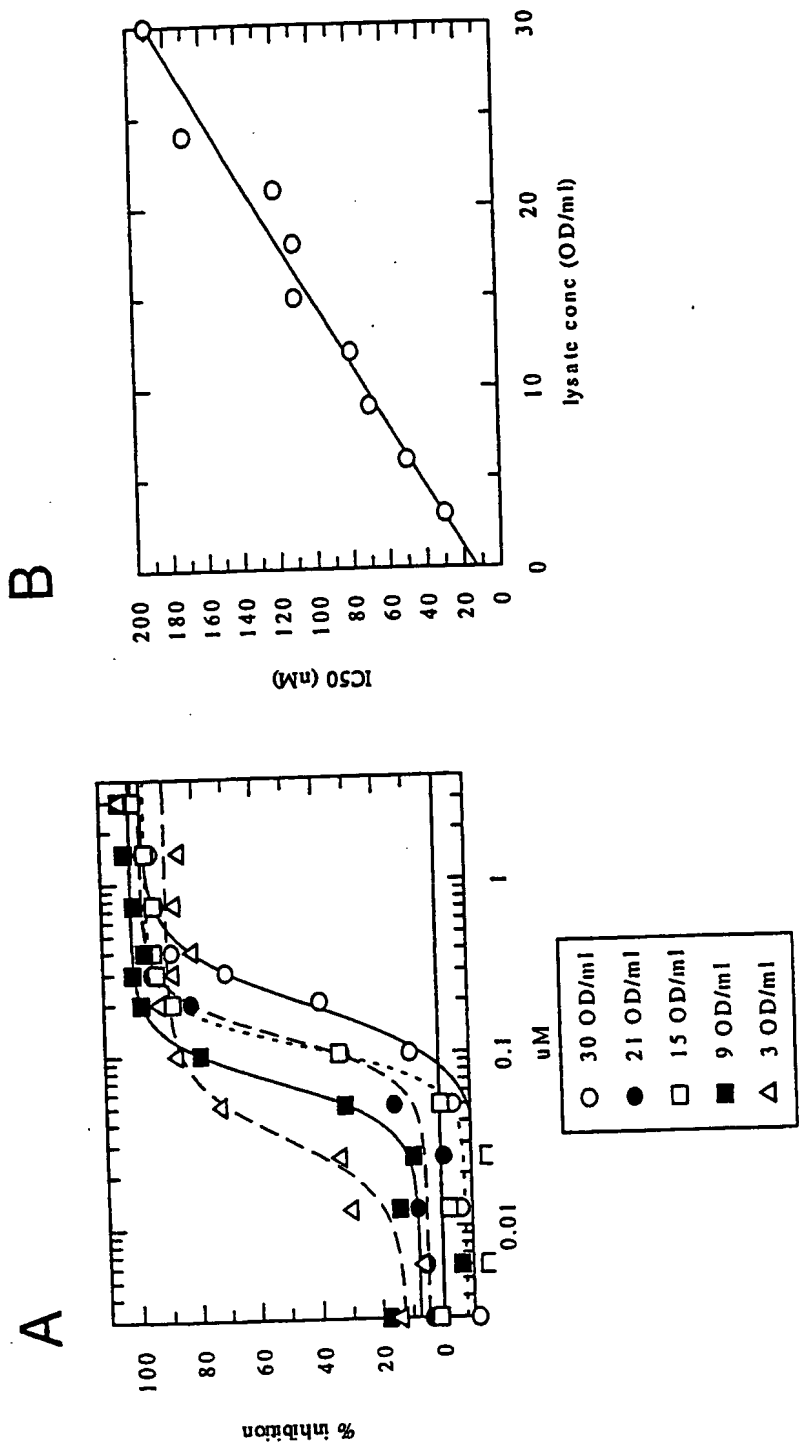


Figure 19.

SB Compound	<i>S. aureus</i> Oxford MICs ( $\mu\text{g/mL}$ )	Radioligand Binding (RLB) IC50 ( $\mu\text{M}$ )	S30 [3H] fmet IC50 ( $\mu\text{M}$ )	S30 Coupled Transcription/Translation IC50 ( $\mu\text{M}$ )
A	$\leq 0.06$	$0.57 \pm 0.04$	$0.25 \pm 0.03$	$0.5 \pm 0.1$
J	$\leq 0.06$	$0.99 \pm 0.09$	$0.18 \pm 0.02$	$1.4 \pm 0.2$
K	0.125	$0.43 \pm 0.09$	$0.19 \pm 0.03$	$0.45 \pm 0.08$
L	0.125	$0.7 \pm 0.1$	$0.5 \pm 0.1$	$0.58 \pm 0.09$
M	4	$7.4 \pm 0.5$	$1.4 \pm 0.5$	$1.5 \pm 0.2$
N	2	$1.3 \pm 0.2$	$0.28 \pm 0.05$	$2.3 \pm 0.4$
E	2	$1.8 \pm 0.4$	$1.6 \pm 0.08$	$1.8 \pm 0.2$
F	2	$2.7 \pm 0.4$	nd	$0.4 \pm 0.1$
G	2	$1.1 \pm 0.5$	$0.27 \pm 0.07$	$0.7 \pm 0.08$
O	4	$8 \pm 1$	$1.4 \pm 0.7$	$1.8 \pm 0.3$
P	4	$0.8 \pm 0.3$	$0.47 \pm 0.08$	$1.2 \pm 0.2$
H	$>64$	$12 \pm 3$	nd	$49 \pm 7$
I	8	$18 \pm 4$	50% at 50 $\mu\text{M}$	$1.1 \pm 0.2$
Q	$>4$	$2.5 \pm 0.3$	$1.2 \pm 0.2$	$2.6 \pm 0.3$
R	$>64$	$>250$	$>250$	$>250$
S	32	$24 \pm 9$	$6 \pm 2$	$31 \pm 4$
Correlation versus MICs (R value from linear regression)	xx	0.69	0.99	0.79
Correlation versus RLB (R value from linear regression fit)	xx	xx	0.98	0.99

Fig 20.



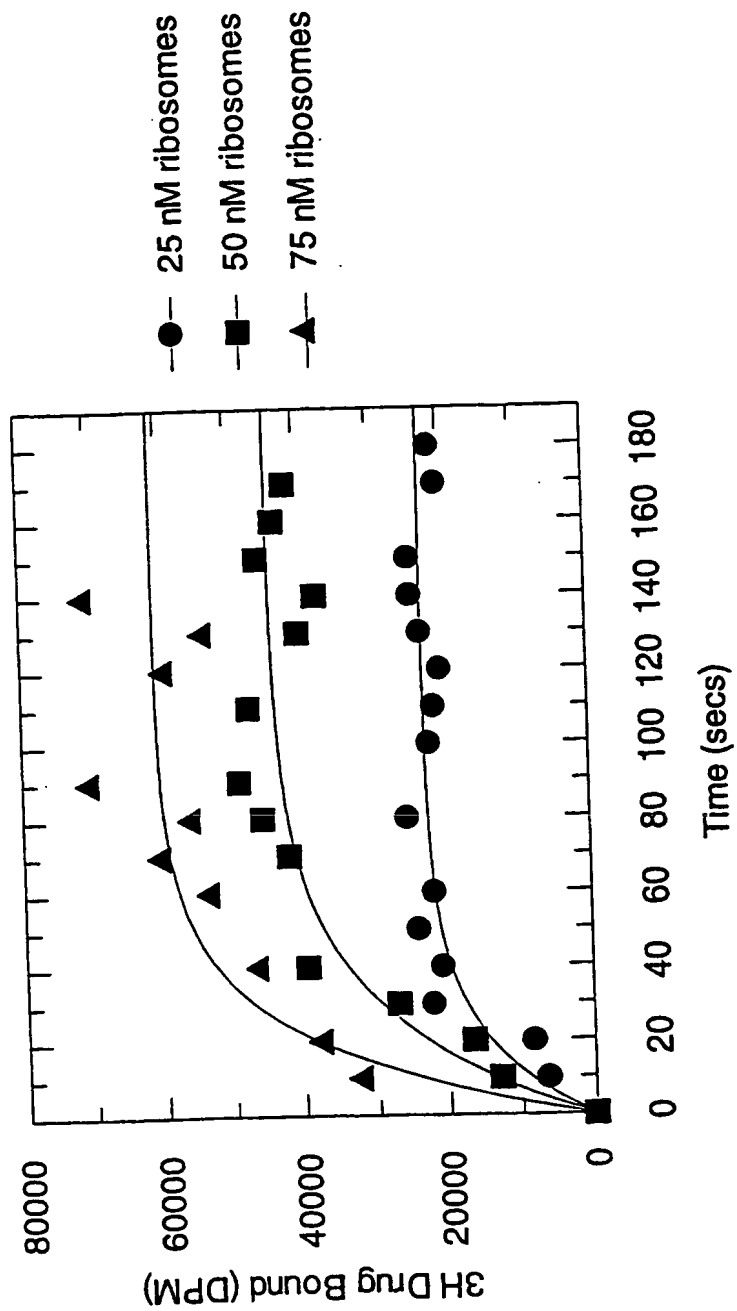
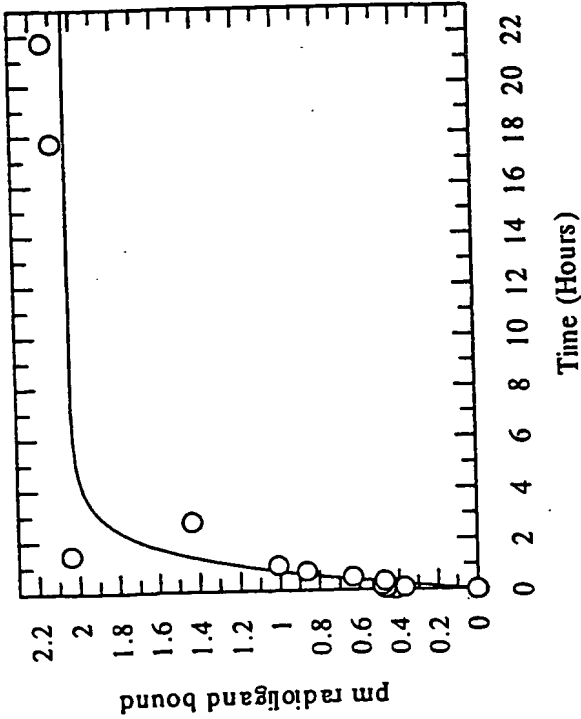


Figure 22.

**B**

SB compound	<i>S. aureus</i> MIC (ug/mL)	$k_{dissociation}$	$t_{1/2}$ (min)
A	$\leq 0.06$		$> 8 \times 60$
E	2	0.38	108
F	2	1.1	40
M	4	0.9	46
Q	$> 4$	0.64	60
U	4	0.72	58

**A**



**Figure 23.**